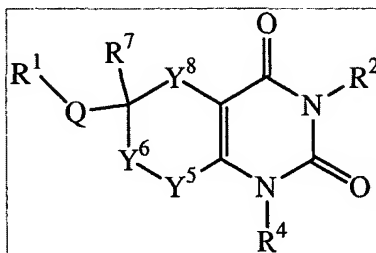


CLAIMS

What is claimed is:

5

1. A compound of Formula I



I

or a pharmaceutically acceptable salt thereof,

wherein:

10

R¹ is independently selected from:

C₅ or C₆ cycloalkyl-(C₁-C₈ alkylenyl);

Substituted C₅ or C₆ cycloalkyl-(C₁-C₈ alkylenyl);

C₈-C₁₀ bicycloalkyl-(C₁-C₈ alkylenyl);

Substituted C₈-C₁₀ bicycloalkyl-(C₁-C₈ alkylenyl);

15

5- or 6-membered heterocycloalkyl-(C₁-C₈ alkylenyl);

Substituted 5- or 6-membered heterocycloalkyl-(C₁-C₈ alkylenyl);

8- to 10-membered heterobicycloalkyl-(C₁-C₈ alkylenyl);

Substituted 8- to 10-membered heterobicycloalkyl-(C₁-C₈ alkylenyl);

Phenyl-(C₁-C₈ alkylenyl);

20

Substituted phenyl-(C₁-C₈ alkylenyl);

Naphthyl-(C₁-C₈ alkylenyl);

Substituted naphthyl-(C₁-C₈ alkylenyl);

5- or 6-membered heteroaryl-(C₁-C₈ alkylenyl);

Substituted 5- or 6-membered heteroaryl-(C₁-C₈ alkylenyl);

25

8- to 10-membered heterobiaryl-(C₁-C₈ alkylenyl);

Substituted 8- to 10-membered heterobiaryl-(C₁-C₈ alkylenyl);

Phenyl;

Substituted phenyl;

Naphthyl;

Substituted naphthyl;
5- or 6-membered heteroaryl;
Substituted 5- or 6-membered heteroaryl;
8- to 10-membered heterobiaryl; and
5 Substituted 8- to 10-membered heterobiaryl;

R² is independently selected from:

- H;
C₁-C₆ alkyl;
Phenyl-(C₁-C₈ alkylenyl);
10 Substituted phenyl-(C₁-C₈ alkylenyl);
Naphthyl-(C₁-C₈ alkylenyl);
Substituted naphthyl-(C₁-C₈ alkylenyl);
5- or 6-membered heteroaryl-(C₁-C₈ alkylenyl);
Substituted 5- or 6-membered heteroaryl-(C₁-C₈ alkylenyl);
15 8- to 10-membered heterobiaryl-(C₁-C₈ alkylenyl);
Substituted 8- to 10-membered heterobiaryl-(C₁-C₈ alkylenyl);
Phenyl-O-(C₁-C₈ alkylenyl);
Substituted phenyl-O-(C₁-C₈ alkylenyl);
Phenyl-S-(C₁-C₈ alkylenyl);
20 Substituted phenyl-S-(C₁-C₈ alkylenyl);
Phenyl-S(O)-(C₁-C₈ alkylenyl);
Substituted phenyl-S(O)-(C₁-C₈ alkylenyl);
Phenyl-S(O)₂-(C₁-C₈ alkylenyl); and
Substituted phenyl-S(O)₂-(C₁-C₈ alkylenyl);
25 Each substituted R¹ and R² group contains from 1 to 4 substituents, each
independently on a carbon or nitrogen atom, independently selected from:
C₁-C₆ alkyl;
CN;
CF₃;
30 HO;
(C₁-C₆ alkyl)-O;
(C₁-C₆ alkyl)-S(O)₂;
H₂N;

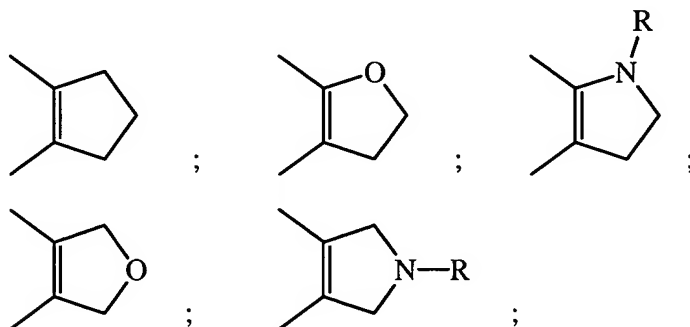
- (C₁-C₆ alkyl)-N(H);
 (C₁-C₆ alkyl)₂-N;
 (C₁-C₆ alkyl)-C(O)O-(C₁-C₈ alkylenyl)_m;
 (C₁-C₆ alkyl)-C(O)O-(1- to 8-membered heteroalkylenyl)_m;
 5 (C₁-C₆ alkyl)-C(O)N(H)-(C₁-C₈ alkylenyl)_m;
 (C₁-C₆ alkyl)-C(O)N(H)-(1- to 8-membered heteroalkylenyl)_m;
 H₂NS(O)₂-(C₁-C₈ alkylenyl);
 (C₁-C₆ alkyl)-N(H)S(O)₂-(C₁-C₈ alkylenyl)_m;
 (C₁-C₆ alkyl)₂-NS(O)₂-(C₁-C₈ alkylenyl)_m;
 10 3- to 6-membered heterocycloalkyl-(G)_m;
 Substituted 3- to 6-membered heterocycloalkyl-(G)_m;
 5- or 6-membered heteroaryl-(G)_m;
 Substituted 5- or 6-membered heteroaryl-(G)_m;
 (C₁-C₆ alkyl)-S(O)₂-N(H)-C(O)-(C₁-C₈ alkylenyl)_m; and
 15 (C₁-C₆ alkyl)-C(O)-N(H)-S(O)₂-(C₁-C₈ alkylenyl)_m;

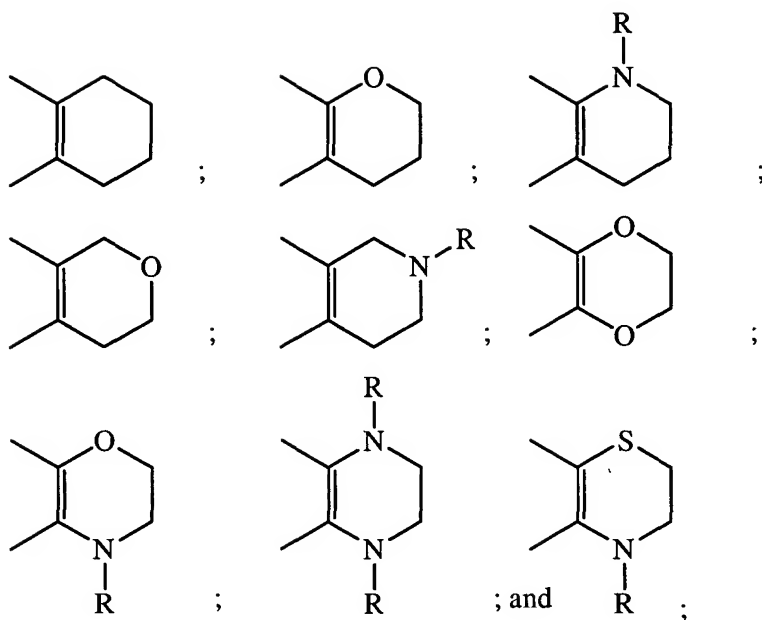
wherein each substituent on a carbon atom may further be independently selected from:

Halo; and

HO₂C;

- 20 wherein 2 substituents may be taken together with a carbon atom to which they are both bonded to form the group C=O;
 wherein two adjacent, substantially sp² carbon atoms may be taken together with a diradical substituent to form a cyclic diradical selected from:





R is H or C₁-C₆ alkyl;

5 G is CH₂; O, S, S(O); or S(O)₂;

m is an integer of 0 or 1;

R⁷ is independently selected from the groups:

- H;
- CH₃;
- 10 CH₃O;
- CH=CH₂;
- HO;
- CF₃;
- CN;
- 15 HC(O);
- CH₃C(O);
- HC(NOH);
- H₂N;
- (CH₃)-N(H);
- 20 (CH₃)₂-N;
- H₂NC(O);
- (CH₃)-N(H)C(O);
- (CH₃)₂-NC(O);

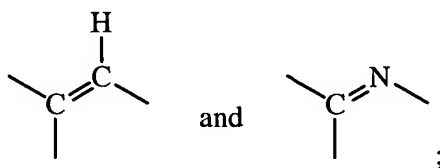
halo; and

CO₂H;

Y⁵ and Y⁸ are each independently CH₂, C(O), O, S, S(O), S(O)₂, or N(R⁵); or

R⁷ and Y⁸ may be taken together with the carbon atom to which they are both

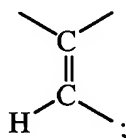
5 attached to form a group selected from:



Y⁶ is CH₂ or C(O); or

Y⁶ and R⁷ may be taken together with the carbon atom to which they are both

attached to form a group:



10

wherein R⁷ is not simultaneously taken together with Y⁶ and Y⁸;

R⁴ and R⁵ are each independently selected from the groups:

H;

CH₃;

15

CH₃O;

CH=CH₂;

HO;

CF₃;

CN;

20

HC(O);

CH₃C(O);

HC(NOH);

H₂N;

(CH₃)-N(H);

25

(CH₃)₂-N;

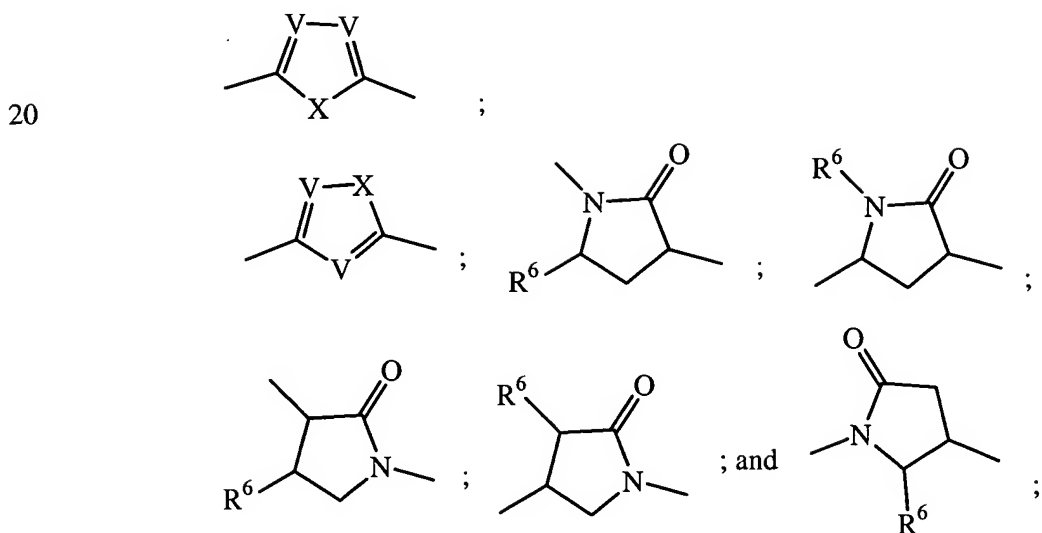
H₂NC(O);

(CH₃)-N(H)C(O); and

(CH₃)₂-NC(O);

Q is selected from:

- OC(O);
 CH(R⁶)C(O);
 OC(NR⁶);
 5 CH(R⁶)C(NR⁶);
 N(R⁶)C(O);
 N(R⁶)C(S);
 N(R⁶)C(NR⁶);
 N(R⁶)CH₂;
 10 SC(O);
 CH(R⁶)C(S);
 SC(NR⁶);
 trans-(H)C=C(H);
 cis-(H)C=C(H);
 15 C≡C;
 CH₂C≡C;
 C≡CCH₂;
 CF₂C≡C; and
 C≡CCF₂;



Each R⁶ independently is H, C₁-C₆ alkyl, C₃-C₆ cycloalkyl; 3- to 6-membered heterocycloalkyl; phenyl; benzyl; or 5- or 6-membered heteroaryl;
 X is O, S, N(H), or N(C₁-C₆ alkyl);

Each V is independently C(H) or N;

wherein each C₈-C₁₀ bicycloalkyl is a bicyclic carbocyclic ring that contains 8-, 9-, or 10-member carbon atoms which are 5,5-fused, 6,5-fused, or 6,6-fused bicyclic rings, respectively, and wherein the ring is saturated or optionally contains one carbon-carbon double bond;

wherein each 8- to 10-membered heterobicycloalkyl is a bicyclic ring that contains carbon atoms and from 1 to 4 heteroatoms independently selected from 2 O, 1 S, 1 S(O), 1 S(O)₂, 1 N, 4 N(H), and 4 N(C₁-C₆ alkyl), and wherein when two O atoms or one O atom and one S atom are present, the two O atoms or one O atom and one S atom are not bonded to each other, and wherein the ring is saturated or optionally contains one carbon-carbon or carbon-nitrogen double bond, and wherein the heterobicycloalkyl is a 5,5-fused, 6,5-fused, or 6,6-fused bicyclic ring, respectively,

wherein each heterocycloalkyl is a ring that contains carbon atoms and from 1 to 4 heteroatoms independently selected from 2 O, 1 S, 1 S(O), 1 S(O)₂, 1 N, 4 N(H), and 4 N(C₁-C₆ alkyl), and wherein when two O atoms or one O atom and one S atom are present, the two O atoms or one O atom and one S atom are not bonded to each other, and wherein the ring is saturated or optionally contains one carbon-carbon or carbon-nitrogen double bond;

wherein each 5-membered heteroaryl contains carbon atoms and from 1 to 4 heteroatoms independently selected from 1 O, 1 S, 1 N(H), 1 N(C₁-C₆ alkyl), and 4 N, and each 6-membered heteroaryl contains carbon atoms and 1 or 2 heteroatoms independently selected from N, N(H), and N(C₁-C₆ alkyl), and 5- and 6-membered heteroaryl are monocyclic rings;

wherein each heterobiaryl contains carbon atoms and from 1 to 4 heteroatoms independently selected from 1 O, 1 S, 1 N(H), 1 N(C₁-C₆ alkyl), and 4 N, and where the 8-, 9-, and 10-membered heterobiaryl are 5,5-fused, 6,5-fused, and 6,6-fused bicyclic rings, respectively, and wherein at least 1 of the 2 fused rings of a bicyclic ring is aromatic, and wherein when the O and S atoms both are present, the O and S atoms are not bonded to each other;

wherein with any (C₁-C₆ alkyl)₂-N group, the C₁-C₆ alkyl groups may be optionally taken together with the nitrogen atom to which they are attached to form a 5- or 6-membered heterocycloalkyl; and wherein each group and each substituent recited above is independently selected.

5

2. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein Y⁶ is C(=O).

10

3. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein Y⁶ is CH₂.

4. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein Q is N(R⁶)C(O).

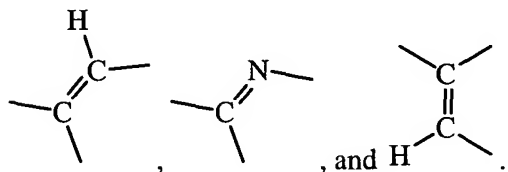
15

5. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein Q is C≡C.

6. The compound according to Claim 1, wherein R⁷ is H.

20

7. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein R⁷ and Y⁸ are taken together with the carbon atom to which they are both attached to form a group selected from:



25

8. The compound according to any one of Claims 1 to 7, or a pharmaceutically acceptable salt thereof, wherein R¹ is independently selected from:

Phenyl-(C₁-C₈ alkylene);

Substituted phenyl-(C₁-C₈ alkylene);

30

5- or 6-membered heteroaryl-(C₁-C₈ alkylene);

Substituted 5- or 6-membered heteroaryl-(C₁-C₈ alkylenyl);
 8- to 10-membered heterobiaryl-(C₁-C₈ alkylenyl); and
 Substituted 8- to 10-membered heterobiaryl-(C₁-C₈ alkylenyl); and

R² is independently selected from:

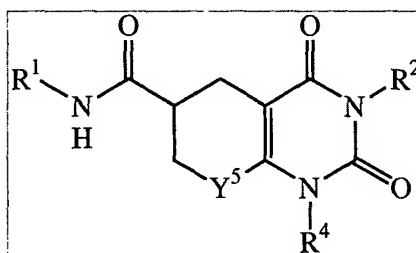
- 5 Phenyl-(C₁-C₈ alkylenyl)_m;
 Substituted phenyl-(C₁-C₈ alkylenyl)_m;
 5- or 6-membered heteroaryl-(C₁-C₈ alkylenyl)_m;
 Substituted 5- or 6-membered heteroaryl-(C₁-C₈ alkylenyl)_m;
 8- to 10-membered heterobiaryl-(C₁-C₈ alkylenyl)_m; and
 10 Substituted 8- to 10-membered heterobiaryl-(C₁-C₈ alkylenyl)_m;

wherein m is an integer of 0 or 1; and

wherein each group and each substituent is independently selected.

9. A compound of Formula II

15



II

or a pharmaceutically acceptable salt thereof.

10. The compound of Formula II according to Claim 9, selected from:

20

3-(3,5-Difluoro-4-hydroxy-benzyl)-1-methyl-2,4-dioxo-1,3,4,5,6,7-hexahydro-2H-thiopyrano[2,3-d]pyrimidine-6-carboxylic acid (2-methoxy-pyridin-4-ylmethyl)-amide;

3-Benzyl-1-methyl-2,4-dioxo-1,3,4,5,6,7-hexahydro-2H-thiopyrano[2,3-d]pyrimidine-6-carboxylic acid 3-methoxy-benzylamide;

25

3-(3,4-Difluoro-benzyl)-1-methyl-2,4-dioxo-1,3,4,5,6,7-hexahydro-2H-thiopyrano[2,3-d]pyrimidine-6-carboxylic acid (pyridin-4-ylmethyl)-amide;

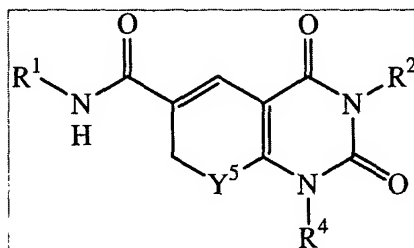
3-Benzyl-1-methyl-2,4-dioxo-1,3,4,5,6,7-hexahydro-2H-thiopyrano[2,3-d]pyrimidine-6-carboxylic acid (pyridin-4-ylmethyl)-amide;

3-Benzyl-1-methyl-2,4-dioxo-1,3,4,5,6,7-hexahydro-2H-thiopyrano[2,3-d]pyrimidine-6-carboxylic acid (2-methoxy-pyridin-4-ylmethyl)-amide; and

3-(3,4-Difluoro-benzyl)-1-methyl-2,4-dioxo-1,3,4,5,6,7-hexahydro-2H-thiopyrano[2,3-d]pyrimidine-6-carboxylic acid (2-methoxy-pyridin-4-ylmethyl)-amide;

or a pharmaceutically acceptable salt thereof.

11. A compound of Formula III



III

or a pharmaceutically acceptable salt thereof.

12. The compound of Formula III according to Claim 11, selected from:

3-(3,5-Difluoro-4-hydroxy-benzyl)-8-methyl-2,4-dioxo-1,2,3,4,7,8-hexahydro-pyrido[2,3-d]pyrimidine-6-carboxylic acid (2-methoxy-pyridin-4-ylmethyl)-amide;

3-Benzyl-8-methyl-2,4-dioxo-1,2,3,4,7,8-hexahydro-pyrido[2,3-d]pyrimidine-6-carboxylic acid 3-methoxy-benzylamide;

3-(3,4-Difluoro-benzyl)-8-methyl-2,4-dioxo-1,2,3,4,7,8-hexahydro-pyrido[2,3-d]pyrimidine-6-carboxylic acid (pyridin-4-ylmethyl)-amide;

3-Benzyl-8-methyl-2,4-dioxo-1,2,3,4,7,8-hexahydro-pyrido[2,3-d]pyrimidine-6-carboxylic acid (pyridin-4-ylmethyl)-amide;

3-Benzyl-8-methyl-2,4-dioxo-1,2,3,4,7,8-hexahydro-pyrido[2,3-d]pyrimidine-6-carboxylic acid (2-methoxy-pyridin-4-ylmethyl)-amide;

- 3-(3,4-Difluoro-benzyl)-8-methyl-2,4-dioxo-1,2,3,4,7,8-hexahydro-
pyrido[2,3-d]pyrimidine-6-carboxylic acid (2-methoxy-pyridin-4-
ylmethyl)-amide;
- 5 3-[4-(3-Ethyl-ureido)-benzyl]-8-methyl-2,4-dioxo-1,2,3,4,7,8-hexahydro-
pyrido[2,3-d]pyrimidine-6-carboxylic acid (2-methoxy-pyridin-4-
ylmethyl)-amide;
- 3-(3,4-Difluoro-benzyl)-8-methyl-2,4-dioxo-1,2,3,4,5,6,7,8-octahydro-
pyrido[2,3-d]pyrimidine-6-carboxylic acid 4-fluoro-benzylamide;
- 10 3-Benzyl-8-methyl-2,4-dioxo-1,2,3,4,7,8-hexahydro-pyrido[2,3-
d]pyrimidine-6-carboxylic acid 4-fluoro-benzylamide; and
- 3-(4-Cyano-benzyl)-8-methyl-2,4-dioxo-1,2,3,4,7,8-hexahydro-pyrido[2,3-
d]pyrimidine-6-carboxylic acid 4-fluoro-benzylamide;
- or a pharmaceutically acceptable salt thereof.
- 15 13. A pharmaceutical composition, comprising a compound according to
Claim 1, or a pharmaceutically acceptable salt thereof, admixed with a
pharmaceutically acceptable carrier, excipient, or diluent.
- 20 14. The pharmaceutical composition according to Claim 13, comprising a
compound according to Claim 10 or 12, or a pharmaceutically acceptable salt
thereof, admixed with a pharmaceutically acceptable carrier, excipient, or diluent.
- 25 15. A method for treating arthritis, comprising administering to a patient
suffering from an arthritis disease a nontoxic antiarthritic effective amount of a
compound according to Claim 1, or a pharmaceutically acceptable salt thereof.
16. The method according to Claim 15, wherein the arthritis is osteoarthritis or
rheumatoid arthritis.
- 30 17. The method according to Claim 16, wherein the compound according to
Claim 1 is a compound according to Claim 10 or 12.